Claims

1. A substrate for the controlled wetting of predetermined wetting sites with small fluid volumes, having

   - a support plate having a horizontal main surface for wetting with a fluid at predetermined wetting sites, and

   - applied to the support plate, a flat protective layer that separates the main surface from the surroundings,

   the protective layer

   - exhibiting, extending to the main surface of the support plate, vertical recesses that define the predetermined wetting sites on the support plate, and

   - including, leading to the vertical recesses, one or more supply channels having reduced thickness in the flat protective layer, for supplying the wetting fluid to the predetermined wetting sites.

2. The substrate according to claim 1, characterized in that the vertical recesses are disposed in the supply channel or supply channels.

3. The substrate according to claim 1 or 2, characterized in that each vertical recess lies in exactly one supply channel.

4. The substrate according to claim 1 or 2, characterized in that each vertical recess lies at the intersection point of multiple, preferably of exactly two supply channels.

5. The substrate according to claim 4, characterized in that at one intersection point of two or more supply channels lies one group of multiple vertical recesses each.

6. The substrate according to one of the preceding claims, characterized in that the vertical recesses or groups of recesses are disposed in the form of an n x m matrix having n rows and m columns, n and m being greater than or equal to 2, and n and m each preferably lying between 10 and 1000.

7. The substrate according to claim 6, characterized **in that** the number n of rows and the number m of columns are identical, and/or that the lateral spacings between adjacent recesses or groups of recesses are identical in the rows and columns.

8. The substrate according to claim 6 or 7, characterized in that the m recesses or groups of recesses in one row are each disposed in one of n parallel row supply channels.

9. The substrate according to claim 8, characterized in that the n recesses or groups of recesses in one column are each disposed in one of m parallel column supply channels, so that each recess lies at the intersection point of two supply channels.

10. The substrate according to claim 9, characterized in that

the row supply channels and the column supply channels exhibit an identical cross-sectional shape.

11. The substrate according to claim 6 or 7, characterized in that each one n' x m' sub-matrix of recesses or groups of recesses is disposed in one meander-shaped supply channel, wherein $n = k_n * n'$ and $m = k_m * m'$, with integers k_n and k_m being greater than or equal to 1.

12. The substrate according to one of the preceding claims, characterized in that compared with the thickness of the protective layer outside the recesses and supply channels, the thickness of the protective layer in the supply channels is reduced by 10% to 99%, preferably by 20% to 95%, particularly preferably by 50% to 95%.

13. The substrate according to one of the preceding claims, characterized in that the protective layer outside the recesses and supply channels exhibits a thickness d_S between 50 µm and 200 µm, preferably between 100 µm and 150 µm.

14. The substrate according to one of the preceding claims, characterized in that the protective layer in the supply channels exhibits a reduced thickness d_K between 5 µm and 150 µm, preferably between about 10 µm and about 50 µm.

15. The substrate according to one of the preceding claims, characterized in that

the supply channels run substantially parallel to the main surface of the support plate.

16. The substrate according to one of the preceding claims, characterized in that the supply channels exhibit a rectangular or trapezoidal cross section.

17. The substrate according to one of the preceding claims, characterized in that the supply channels exhibit a characteristic width b_K between 5 µm and 250 µm, preferably of about 10 µm to about 150 µm.

18. The substrate according to one of the preceding claims, characterized in that the wetting sites exhibit a characteristic dimension of about 5 µm to about 200 µm, preferably of about 10 µm to about 100 µm.

19. The substrate according to one of the preceding claims, characterized in that the vertical recesses exhibit a substantially rectangular, elliptical or circular cross section.

20. The substrate according to one of the preceding claims, characterized in that the protective layer consists of a material that physisorbs or chemisorbs on the support plate main surface to be wetted, or binds to it covalently, coordinatively or by complex formation.

21. The substrate according to one of the preceding claims,

characterized in that
the protective layer is formed by a positive or negative photoresist, a solder resist or an organic polymer, especially cellulose, dextran or collagen.

22. The substrate according to one of the preceding claims,
characterized in that
the support plate exhibits a base plate consisting of plastic, metal, semiconductor, glass, composite or a porous material, or a combination of these materials, the support plate in the case of a non-conductive base plate preferably being provided with a conductive layer, especially consisting of silicon, platinum or gold, which then forms the support plate main surface to be wetted.

23. The substrate according to one of the preceding claims,
characterized in that
the predetermined wetting sites are functionalized with specific probe molecules, especially in that, at the predetermined wetting sites, probe molecules are physisorbed or chemisorbed on the support plate main surface, or are bound to it covalently, coordinatively or by complex formation.

24. The substrate according to claim 23, characterized in that
the predetermined wetting sites are functionalized with nucleic acid oligomers that are modified with one or more reactive groups.

25. The substrate according to claim 22 and 24, characterized in that
the support plate main surface to be wetted is formed by a gold layer and the predetermined wetting sites are functionalized with thiol- (HS-) or disulfide- (S-S-) derivatized nucleic acid oligomers.

26. The substrate according to claim 24 or 25, characterized in that the nucleic acid oligomers are modified with a fluorophore.

27. The substrate according to one of the preceding claims, characterized in that the substrate is covered with a cover plate that closes the supply channels in the up direction to form flow chambers.

28. A substrate for the controlled wetting of predetermined wetting sites with small fluid volumes, having

- a support plate having a horizontal main surface for wetting with a fluid at predetermined wetting sites, and

- applied to the support plate, a flat protective layer that separates the main surface from the surroundings,

the protective layer

- including one or more depressions having reduced thickness in the flat protective layer for taking up a reservoir volume of wetting fluids, and

- exhibiting, disposed in the depressions, extending to the main surface of the support plate, vertical recesses that define the predetermined wetting sites on the support plate, and that take up the wetting fluids of the respective depressions.

29. The substrate according to claim 28, characterized in that

the vertical recesses are disposed in the form of an n x m matrix having n rows and m columns, n and m being greater than or equal to 2, and n and m each preferably lying between 4 and 20.

30. The substrate according to claim 28 or 29, characterized in that the number n of rows and the number m of columns are identical, and/or that the lateral spacings between adjacent recesses are identical in the rows and columns.

31. The substrate according to one of claims 28 to 30, characterized in that compared with the thickness of the protective layer outside the recesses and depressions, the thickness of the protective layer in the depressions is reduced by 10% to 99%, preferably by 20% to 95%, particularly preferably by 50% to 95%.

32. The substrate according to one of claims 28 to 31, characterized in that the protective layer outside the recesses and depressions exhibits a thickness d_S between 50 µm and 200 µm, preferably between 100 µm and 150 µm.

33. The substrate according to one of claims 28 to 32, characterized in that the protective layer in the depressions exhibits a reduced thickness d_K between 5 µm and 150 µm, preferably between about 10 µm and about 50 µm.

34. The substrate according to one of claims 28 to 33,

characterized in that

the depressions exhibit a rectangular or trapezoidal cross section.

35. The substrate according to one of claims 28 to 34,

characterized in that

the depressions exhibit a characteristic dimension A_K between 100 µm and 2000 µm, preferably of about 300 µm to about 1000 µm.

36. The substrate according to one of claims 28 to 35,

characterized in that

the wetting sites exhibit a characteristic dimension of about 5 µm to about 200 µm, preferably of about 10 µm to about 100 µm.

37. The substrate according to one of claims 27 to 36,

characterized in that

the vertical recesses exhibit a substantially rectangular, elliptical or circular cross section.

38. The substrate according to one of claims 28 to 37,

characterized in that

the protective layer consists of a material that physisorbs or chemisorbs on the support plate main surface to be wetted, or binds to it covalently, coordinatively or by complex formation.

39. The substrate according to one of claims 28 to 38,

characterized in that

the protective layer is formed by a positive or negative photoresist, a solder resist or an organic polymer, especially cellulose, dextran or collagen.

40. The substrate according to one of claims 28 to 39,
characterized in that
the support plate exhibits a base plate consisting of plastic, metal, semiconductor, glass, composite or a porous material, or a combination of these materials, the support plate in the case of a non-conductive base plate preferably being provided with a conductive layer, especially consisting of silicon, platinum or gold, which then forms the support plate main surface to be wetted.

41. The substrate according to one of claims 28 to 40,
characterized in that
the predetermined wetting sites are functionalized with specific probe molecules, especially in that, at the predetermined wetting sites, probe molecules are physisorbed or chemisorbed on the support plate main surface, or are bound to it covalently, coordinatively or by complex formation.

42. The substrate according to claim 41, characterized in that
the predetermined wetting sites are functionalized with nucleic acid oligomers that are modified with one or more reactive groups.

43. The substrate according to claim 40 and 42, characterized in that
the support plate main surface to be wetted is formed by a gold layer and the predetermined wetting sites are functionalized with thiol- (HS-) or disulfide- (S-S-) derivatized nucleic acid oligomers.

44. The substrate according to claim 42 or 43, characterized in that
the nucleic acid oligomers are modified with a fluorophore.

45. A substrate covering for a substrate according to one of claims 1 to 27 having a covering support plate having a plurality of protruding barrier elements whose shape and size are matched with the shape and size of the supply channels of the substrate to close the supply channels in sub-regions.

46. The substrate covering according to claim 45 for a substrate according to claim 10, characterized in that
the barrier elements are disposed on the covering support plate such that, after the joining of the substrate covering with the substrate, they close only the row supply channels or only the column supply channels.

47. A flow chamber having a substrate according to one of claims 1 to 27 and a substrate covering according to claim 45 or 46 that is permanently or detachably joined with the substrate.

48. The flow chamber according to claim 47, characterized in that

- the arrangement of the recesses and of the supply channels of the substrate exhibits a multifold symmetry, and
- the barrier elements of the substrate covering are disposed on the covering support plate such that the substrate covering is placeable in various orientations on the substrate and thereby closes different sub-regions of the supply channels.

49. The flow chamber according to claim 48 having a substrate according to claim 10, in which the substrate covering covers, in a first orientation, the

row supply channels, and in a second orientation rotated 90° against the first orientation, the column supply channels.

50. A method for manufacturing a substrate for the controlled wetting of predetermined wetting sites with small fluid volumes, especially according to one of claims 1 to 27, comprising the steps:

a) providing a support plate having a horizontal main surface,

b) applying to the support plate a flat protective layer that separates the main surface from the surroundings,

c) patterning the protective layer to create one or more supply channels having a reduced protective layer thickness, and

d) creating in the supply channel or supply channels vertical recesses that extend to the main surface of the support plate and define the predetermined wetting sites on the main surface of the support plate.

51. A method for manufacturing a substrate for the controlled wetting of predetermined wetting sites with small fluid volumes, especially according to one of claims 28 to 44, comprising the steps:

a) providing a support plate having a horizontal main surface,

b) applying to the support plate a flat protective layer that separates the main surface from the surroundings,

c) patterning the protective layer to create a depression having a reduced protective layer thickness, and

d) creating in the depression vertical recesses that extend to the main surface of the support plate and define the predetermined wetting sites on the main surface of the support plate.

52. The method according to claim 50 or 51, characterized in that as the protective layer, a solder resist is applied with a curtain coating method.

53. The method according to one of claims 50 to 52, characterized in that the recesses and/or the supply channels or the depression are created by means of laser ablation, especially by irradiation of sub-regions of the protective layer with continuous or pulsed laser radiation of a predetermined wavelength, preferably in the ultraviolet spectral range.

54. The method according to claim 53, characterized in that in creating the recesses in step d), a surface region of the support plate is melted in the region of the wetting sites.

55. The method according to one of claims 50 to 54, characterized in that in a step e), the predetermined wetting sites are functionalized with specific probe molecules.

56. The method according to claim 55, characterized in that

in step e), the predetermined wetting sites are functionalized with nucleic acid oligomers with a spotting method.

57. The method according to claim 50 and 55, characterized in that in step e), the predetermined wetting sites are functionalized by flushing a solution with nucleic acid oligomers into the supply channels.

58. The method according to claim 51 and 55, characterized in that in step e), the predetermined wetting sites are functionalized by filling the depression with a solution with nucleic acid oligomers.